

Amendments to Specification

Please replace the "Related Applications" paragraph at page 1, lines 6-7 with the following paragraph:

This application is a continuation of Application No. 09/809,739, filed March 15, 2001, now U.S. Patent No. 6,663,863, which is a continuation-in-part of Application No. 09/528,267, filed on March 17, 2000 (abandoned). The entire teachings of each of the foregoing applications are incorporated herein by reference.

Please replace the paragraph at page 12, lines 7-11 with the following paragraph:

Agents which can inhibit the recruitment and/or adhesion of neutrophils and/or mononuclear cells to a site of vascular injury can be identified, for example, by screening libraries or collections of molecules, such as, the Chemical Repository of the National Cancer Institute[®], as described herein or using other suitable methods. Agents thus identified can be used in the therapeutic methods described herein.

Please replace the paragraph starting at page 20, line 3 with the following paragraph:

Other preferred antibodies bind mammalian CCR2 (e.g., human CCR2) and inhibit the binding of a ligand (e.g., MCP-1, MCP-2, MCP-3, MCP-4, MCP-5) to the receptor. Murine monoclonal antibodies designated 1D9 (also referred to as LS132.1D9 or 1D9-2-121-3-6) and 8G2 (also referred to as LS132.8G2), which bind CCR2 and inhibit the binding of ligand to the receptor, were produced as described herein. Hybridoma cell lines producing the antibodies were deposited on July 17, 1998, on behalf of LeukoSite, Inc., 215 First Street, Cambridge, MA 02142, U.S.A., (now Millennium[®] Pharmaceuticals, Inc., 75 Sidney Street, Cambridge, MA 02139, U.S.A.) at the American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110, U.S.A., under Accession Nos. HB-12549 (1D9) and HB-12550 (8G2). These antibodies and, for example, chimeric or humanized version of the antibodies can be administered in accordance with the method of the invention. An antibody which binds CCR2 and inhibits the binding of a ligand (e.g., MCP-1, MCP-2, MCP-3, MCP-4, MCP-5) to the

receptor can comprise a humanized 1D9 light chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17 and SEQ ID NO: 18, and/or a humanized 1D9 heavy chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, and SEQ ID NO: 23. In certain embodiments, an antibody which binds CCR2 and inhibits the binding of a ligand to the receptor can comprise a humanized chain (e.g., a humanized 1D9 light chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17 and SEQ ID NO: 18, or a humanized 1D9 heavy chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, and SEQ ID NO: 23) and a complementary chain (heavy or light as appropriate) which is, for example, human, nonhuman (e.g., rodent (e.g., murine), primate) humanized or chimeric. A complementary light or heavy chain is one which is capable of associating with a selected heavy or light chain, respectively, resulting in an antibody or antigen-binding fragment which binds CCR2 and inhibits the binding of a ligand (e.g., MCP-1, MCP-2, MCP-3, MCP-4, MCP-5) to the receptor. Antigen-binding fragments of such antibodies (e.g., Fab fragments, F(ab')₂ fragments, Fab' fragments, Fv fragments) can also be administered in accordance with the method of the invention.

Please replace the paragraph at page 29, line 7 with the following paragraph:

If desired, the agent(s) which inhibit recruitment and/or activation of neutrophils and/or mononuclear cells to a site of vascular injury can be co-administered with one or more additional therapeutic agents, for example, a fibrinolytic agent (e.g., Retavase), a thrombolytic agent, such as a plasminogen activator (e.g., tissue plasminogen activator, urokinase, streptokinase, recombinant plasminogen activator), anticoagulant (e.g., heparin, hirulog, hirudin, aspirin), or a coumarin anticoagulant (e.g., warfarin, ethyldine dicoumarol), a β -adrenergic blocker (e.g., alprenolol, acebutolol, propranolol), calcium channel blocker (e.g., nifedipine, diltiazem, cinnarizine, flunarizine), gpIIb/IIIa antagonists (e.g., c7E3 Fab (ReoPro®, abciximab, Centocor®, Inc., Malvern, PA)), vasodilator (e.g., nitroglycerin, amotriphene, erythritol, prenylamine) or an agent which stimulates the production of nitric oxide (see, for example, Singh *et al.*, U.S. Pat. No. 5,811,437).

Please replace the paragraph at page 44, lines 12-14 with the following paragraph:

The right carotid artery was surgically exposed and a 6Fr percutaneous vascular introducer sheath (e.g. CP-07711, ARROW® International, Reading, PA 19605) was placed to facilitate interventional catheter placement.

Please replace the paragraph starting at page 44, line 15 with the following paragraph:

Utilizing fluoroscopic guidance, a 6Fr guide catheter was passed antegrade to the level at which the distal abdominal aorta bifurcates into the right and left iliac arteries. A radiopaque 0.014-inch guide wire (e.g. 22225M, Advanced Cardiovascular Systems, Inc., Temecula, CA 92591) was used to facilitate passage of the guide catheter or other catheters as necessary. Radiopaque contrast media (e.g. Omnipaque™, iohexol injection, Nycomed®, Princeton, NJ 75039) was used as necessary to facilitate fluoroscopy.

Please replace the paragraph starting at page 45, line 6 with the following paragraph:

An 80 cm, 3Fr Fogarty balloon embolectomy catheter (e.g. 120803F, Baxter® Healthcare Corp., Irvine, CA 92714) with a balloon appropriately sized for the vessel was passed via the guide catheter into the right iliac artery, to a level about 4 cm distal to the aortic bifurcation. The balloon was then inflated with 0.6 cc air and withdrawn inflated over an about 3 cm section of artery to facilitate endothelial denudation. Balloon angioplasty was performed three times. This procedure was then repeated in the contralateral (left) iliac artery and the balloon embolectomy catheter was withdrawn. In some cases the left iliac artery was denuded first, followed by the right.

Please replace the paragraph starting at page 45, line 15 with the following paragraph:

An appropriate-sized dilation catheter (Ninja™ PTCA dilation catheter with SLX™ coating, Cordis® Corp., Miami FL 33102) fitted with a balloon-expandable 7-mm stent (e.g., one half of a 15-mm long stent (e.g. CS15-030, Palmaz-Schatz® crown balloon-expandable stent, Cordis® Corp., Miami FL 33102)) was then passed into the right iliac artery to the level of

the midpoint of endothelial denudation. The balloon was inflated to the appropriate inflation pressure required to expand the stent sufficiently to provide a balloon/stent:artery ratio of 1.1-1.2 (typically 6 Atm for 2.5, 3.0 or 3.5 mm catheters). The balloon was deflated and the catheter was withdrawn. This procedure was repeated in the contralateral (left) iliac artery. In some cases the left iliac artery was stented first, followed by the right.

Please replace the paragraph starting at page 47, line 8 with the following paragraph:

Animals were already anesthetized for follow-up angiography. Animals were euthanized in accordance with American Veterinary Medical Association (AVMA)³ guidelines³ by deep anesthesia (sodium pentobarbital, 35 mg/kg, IV), followed by exsanguination.

Please replace the paragraph starting at page 50, line 21 with the following paragraph:

Briefly, 96-well plates (NUNC™ #4-39454) were coated with 100 µl goat-anti-mouse IgG +IgM antibody (Jackson ImmunoResearch #115-005-068) at 2.5 µg/ml in carbonate buffer pH 9.3 overnight at 4 °C. Plates were subsequently washed 3 times with PBS 0.5% Tween-20 and blocked with 300 µl PBS / 1% BSA for 60 minutes at 37 °C. Following 3 additional washes with PBS-Tween, serum samples were diluted 1:100 in PBS / 1%BSA and 100 µl aliquots were added to duplicate wells in the plate. The antibody standard (MOPC-21, Sigma) was diluted to 50 ng / ml and 100 µl aliquots were added to the plate. Subsequently, all samples were diluted 2-fold across the plate and incubated at room temperature for 2 hours. The plate was subsequently washed again with PBS / 0.5%Tween-20 and 100 µl of peroxidase-conjugated goat anti-mouse IgG +IgM (Jackson ImmunoResearch #115-035-068) was added at a concentration of 375 ng/ml and incubated for 2 hours at room temperature. Following additional washes with PBS-Tween, plates were developed with o-phenylenediamine (OPD, Sigma®) in citric acid buffer pH 5.0, and analyzed on a 96-well fluorescent plate reader (Dynatech MR4000) at 492 nm. The dilutions of the antibody standard was used to construct a standard curve, and the serum antibody concentration was automatically derived from the standard curve and dilution factor data provided using Bioline 2.22 software.